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Noninvasive Estimation of Regurgitant Flow Rate and Volume in Patients With Mitral Regurgitation by Doppler Color Mapping of Accelerating Flow Field

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Objectives. This study was designed to examine the accuracy of proximal accelerating flow calculations in estimating regurgitant flow rate or volume in patients with different types of mitral valve disease.

Background. Flow acceleration proximal to a regurgitant orifice, observed with Doppler color flow mapping, is constituted by isovelocity surfaces centered at the orifice. By conservation of mass, the flow rate through each isovelocity surface equals the flow rate through the regurgitant orifice.

Methods. Forty-six adults with mitral regurgitation of angiographic grades I to IV were studied. The proximal accelerating flow rate (Q) was calculated by: $Q = 2\pi r^2 \cdot Vn$, where πr^2 is the area of the hemisphere and Vn is the Nyquist velocity. Radius of the hemisphere (r) was measured from two-dimensional or M-mode Doppler color recording. From the M-mode color study, integration of accelerating flow rate throughout systole yielded stroke accelerating flow volume and mean flow rate. Mitral regurgitant flow rate and stroke regurgitant volume were measured by using a combination of pulsed wave Doppler and two-dimensional echocardiographic measurements of aortic forward flow and mitral inflow.

Results. The proximal accelerating flow region was observed in 42 of 46 patients. Maximal accelerating flow measured from either two-dimensional (372 ± 389 ml/s) or M-mode (406 ± 421 ml/s) Doppler color study tended to overestimate the mean regurgitant flow rate (306 ± 253 ml/s, $p < 0.05$). Mean Doppler accelerating flow rate correlated well with mean regurgitant flow rate ($r = 0.95$, $p < 0.001$), although there was a tendency toward slight overestimation of mean regurgitant flow by mean accelerating flow in severe mitral regurgitation. However, there was no significant difference between the mean accelerating flow rate (318 ± 304 ml/s) and the mean regurgitant flow rate (306 ± 253 ml/s, p = NS) for all patients. A similar relation was found between accelerating flow stroke volume (78.27 ± 62.72 ml) and regurgitant flow stroke volume (76.06 ± 59.76 ml) ($r = 0.95$, $p < 0.001$). The etiology of mitral regurgitation did not appear to affect the relation between accelerating flow and regurgitant flow.

Conclusions. Proximal accelerating flow rate calculated by the hemispheric model of the isovelocity surface was applicable and accurate in most patients with mitral regurgitation of a variety of causes. There was slight overestimation of regurgitant flow rate by accelerating flow rate when the regurgitant lesion was more severe.

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Assessment of the morphology of the mitral apparatus and the severity of mitral regurgitation has an important impact on clinical decision-making. Two-dimensional echocardiography provides detailed information about pathologic changes of the mitral apparatus and, thereby, the etiology of mitral regurgitation (1). Doppler color flow mapping allows visualization of regurgitant jets in real time and thus, is the mostly widely used noninvasive tool for grading severity of mitral regurgitation (2–6). However, grading the severity of mitral regurgitation with Doppler color flow mapping provides only a semiquantitative estimation of mitral regurgitation and may lead to significant errors under certain circumstances (6–11), such as the presence of an eccentrically directed wall jet (6), significant variation of blood pressure (8) or inappropriate Doppler color ultrasound machinery settings (7).

Accelerating flow proximal to a restrictive orifice of stenotic, regurgitant and shunt lesions has been observed using Doppler color flow mapping (11–21) and nuclear magnetic resonance imaging (22). This proximal accelerating flow is laminar and relatively free from factors that could change the appearance and size of the downstream regurgi-

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tant jet and thus shows great promise for accurately quantifying mitral regurgitation. It is assumed that the proximal fluid converges uniformly and radially toward an orifice and forms hemispheric isovelocity layers or surfaces. By the conservation of mass, the accelerating flow through each isovelocity surface equals flow through the regurgitant orifice for a regurgitant lesion because all flow through the isovelocity surface must pass through the orifice (16–19,23,24). Initial in vitro, canine model and computational modeling studies (11–21) have shown the validity of the assumption that the proximal isovelocity surfaces have a hemispheric shape for a planar orifice whose diameter is small relative to the radius of the isovelocity hemisphere. Previous clinical studies (19,25) in patients with mitral regurgitation have demonstrated that mitral regurgitant flow rate calculated from the Doppler color flow accelerating region correlated well with semiquantitative angiographic grading of mitral regurgitation. However, it is important to compare mitral regurgitant flow rate estimated by the proximal accelerating field directly with true regurgitant flow rate or volume derived from other independent methods, and to examine the effect of pathologic changes of different causes of mitral regurgitation on the accuracy of estimating regurgitant flow by using the proximal accelerating flow field. Therefore, the purposes of this study were 1) to compare Doppler color study values for accelerating flow rates with mitral regurgitant flow rates; 2) to examine the relation between proximal accelerating flow volume and mitral regurgitant volume; and 3) to examine the effect of different causes of mitral regurgitation on the accuracy of the proximal accelerating flow for estimation of regurgitant flow.

Methods

Patients

The study group comprised 46 consecutive patients studied between February 1991 and February 1992 who had angiographically documented mitral regurgitation and an echocardiogram of adequate quality for measuring mitral inflow, aortic forward flow, mitral regurgitant jet and accelerating flow proximal to the mitral regurgitant orifice. The mean age was 61 ± 16 (range 23 to 85) years. There were 17 women and 29 men. The cause of mitral regurgitation was coronary artery disease in 11 patients, dilated cardiomyopathy in 5, chordal rupture in 6, mitral valve prolapse in 5, rheumatic valve disease in 4 and other causes in 15. Patients with aortic disease, a prosthetic valve or atrial fibrillation were excluded.

Protocol

Echocardiographic studies. Doppler color echocardiography was performed with a commercially available system (Hewlett-Packard Sonos 500 or 1000) equipped with a 2.5-MHz transducer. With this system, flow directed toward the transducer was red-yellow and flow away from it was blue. An optimal gain setting was obtained by maximizing the gain level without introducing spurious signals in the nonflow areas. Medium color wall filter (medium clutter filter) was chosen and remained unchanged for all Doppler color study performed in the cardiac ultrasound laboratories at the University Hospital, Hamburg. The function of spatial filter of scan line smoothing was not used. The frame rate used for color flow imaging in this study was 15 to 18 frames/s with a sector width varying between 30° and 60°. Each examination was performed by using the shallowest depth and narrowest sector angle capable of encompassing the entire jet or proximal accelerating flow area. The pulse repetition frequency was typically between 3.8 and 4.6 kHz. Velocity of flow is represented by the brightness of the colors and is measurable unambiguously until 58 cm/s (Nyquist limit velocity) at the depth of 16 cm. If the velocity is higher, color reversal occurs in the color display. For each study, the point of first aliasing can be altered by zero shifting, and the Nyquist velocity limit for flow away from the transducer was reduced to 19 to 39 cm/s. In the freeze frame of the Doppler color M-mode study, the zero shifting could also be altered. All M-mode, two-dimensional, pulsed wave Doppler and Doppler color flow studies were recorded on 0.5-in. (1.27 cm) videotapes (Panasonic NV-8200) for subsequent analysis.

Pulsed wave Doppler mitral flow recording. Mitral flow was quantified as described previously (6,26–28). First, the mitral valve orifice was imaged in the parasternal short-axis view with the patient in the left lateral position. The transducer was manipulated to image the orifice at the leaflet tips. Two-dimensional echocardiographically guided M-mode echocardiograms of the mitral valve were recorded at the same level. The pulsed Doppler mitral flow profile was obtained from the apical view. The sample volume was placed at the tips of mitral leaflets as parallel as possible to the left ventricular diastolic inflow.

Pulsed wave Doppler aortic flow recording. Two-dimensional echocardiography was performed to image the parasternal long-axis view of the left ventricle and the proximal ascending aorta. The Doppler aortic flow profile was obtained from the apical view where the pulsed Doppler cursor line of the sample volume was parallel to the assumed aortic blood flow direction by Doppler color flow mapping. The sample volume was positioned between the aortic leaflets where the largest Doppler shifts were clearly recorded (6,26–28).

Doppler color flow mapping of regurgitant jet and proximal acceleration zone. Mitral regurgitation was defined by a high velocity systolic jet, represented by Doppler color flow mapping as mosaic color or multireversal color display, through the mitral valve into the left atrium. When mitral regurgitation was observed, the transducer was manipulated to record the proximal accelerating flow region. The proximal accelerating flow field is represented as a homogeneous blue flow pattern, indicating flow directed away from the transducer, of increasing brightness and interrupted with red

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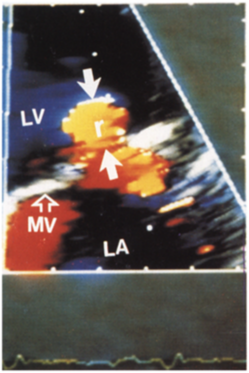


Figure 1. Doppler color two-dimensional recording of a proximal accelerating flow region. The Nyquist velocity for the flow away from the transducer was 29 cm/s as shown on the color scale display at left and the radius of the proximal isovelocity layer (r) was 1.2 cm (the measurement is labeled by two solid arrows) in this case. The distance between 2 dots is 1 cm. In this patient, the downstream regurgitant jet was directed eccentrically to the wall. The wall jet was small on the color Doppler flow mapping. LA = left atrium; LV = left ventricle; MV = mitral valve leaflet.

or yellow interfaces (aliasing) on the ventricular side of the mitral valve, with a central zone at the mitral regurgitant orifice (Fig. 1). Special attention was paid to image proximal acceleration flow of mitral regurgitation using Doppler color scanning in parasternal and apical views. Efforts were made to obtain the maximal proximal acceleration area. 1) The transducer was tilted down and up or rotated from the standard views until the greatest proximal acceleration zone was observed; 2) the ultrasound beam was aligned as parallel as possible to the direction of the regurgitant flow to avoid underestimation of the proximal hemispheric surface velocities; 3) the Nyquist limit velocity was set as low as possible, usually 19 to 39 cm/s, to maximize the visible acceleration zone and to reduce calculation error of the flow rate induced by nonhemispheric morphology of near-orifice isovelocity acceleration surfaces. Caution was taken to avoid inappropriate use of low Nyquist velocity, which can make the accelerating flow region on Doppler color study indistinguishable from interventricular flow. When the maximal proximal acceleration area was observed in Doppler color two-dimensional scanning, the M-mode beam was aligned perpendicular to the center of the acceleration zone and color M-mode recording of the acceleration flow was obtained. Four patients were excluded from this study because of inappropriate alignment of the M-mode ultrasound beam.

Echocardiographic analysis. All measurements were performed with a Hewlett-Packard Sonos 1000 built-in computer analyzing system. Each echocardiographic and Doppler measurement was obtained in three to five different cardiac cycles, and the average was used in subsequent analysis. The angle between the assumed blood flow direction by Doppler color flow mapping and the cursor line of the sample volume was measured with angle correction applied to the Doppler velocities for angles >20°.

Pulsed wave Doppler-derived mitral and aortic forward flow. These measurements are described in detail in previous studies (6,26–28). Briefly, the aortic diameter was measured at the point of insertion of the valve leaflets at early systole. The mitral valve area was measured by tracing the inner edge of the leaflet echoes in short axis from the frame showing maximal opening. The e-e′ (maximal separation of the anterior and posterior mitral leaflets) distance, the d-c (duration of the mitral valve opening) interval and the total

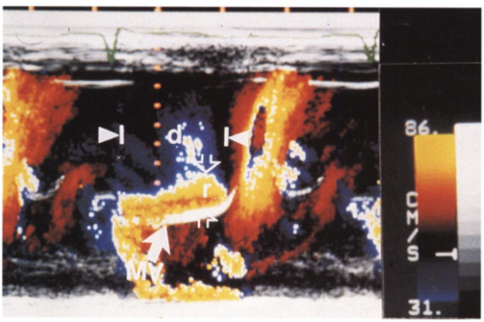


Figure 2. Doppler color M-mode recording of a proximal accelerating flow region. The duration (d) of the systolic accelerating flow proximal to the regurgitant orifice is labeled by two solid triangles. The Nyquist limit velocity for the flow away from the transducer was 31 cm/s (measurement is labeled by two open arrows). The maximal radius (r) of the proximal isovelocity layer was changing during systole. The distance between two dots is 1 cm. The solid arrow points to the mitral valve (MV).

area between the anterior and posterior leaflets during diastole were measured from the M-mode echocardiogram. The mean separation (area between the leaflets divided by the d-c interval) was divided by the maximal leaflet separation (e-e') to give the mean to maximal ratio; the mean diastolic orifice area was obtained by multiplying this ratio by the maximal valve area from two-dimensional planimetry. The Doppler profiles of the aortic (systolic) and mitral (diastolic) velocity spectrum were traced and measured to yield the time-velocity integral with units of distance (cm) using the computer analyzing system. The cardiac cycle length (RR interval) was measured from corresponding simultaneous electrocardiogram and the heart rate calculated. Systolic ejection time and diastolic filling time were measured directly from the beginning to the end of Doppler shifts from the baseline of the aortic and mitral pulsed Doppler profile, respectively.

Regurgitant flow calculations. According to the method described by Fisher et al. (28), the mitral forward flow through each valve was then calculated from the product of the mitral time-velocity integral, mean mitral valve area and heart rate. The aortic outflow was determined as the product of the aortic time-velocity integral, aortic anulus area and heart rate (25). The regurgitant stroke volume was calculated by subtracting aortic flow from mitral forward flow. The mitral regurgitant flow volume (ml/min) was calculated by multiplying regurgitant stroke volume by heart rate. The mean mitral regurgitant flow rate (ml/s) was calculated by dividing regurgitant stroke volume by left ventricular systolic ejection time.

Doppler color proximal acceleration flow. Calculation of proximal accelerating flow has been described in detail previously (12,16,18,19). Briefly, with Doppler color flow mapping it can be observed that flow accelerates before it enters a restricted orifice. This accelerating flow field is constituted by radially converging streamlines toward the orifice. In this study, by assuming hemispheric shape of the isovelocity surface for all patients, flow (Q) through an isovelocity surface was then calculated by:

$$Q = 2\pi r^2 \cdot Vn, \qquad [1]$$

where r is the distance from mitral regurgitant orifice to the first color reversal line between the blue and the yellow-red boundary, as shown in Figures 1 and 2, and Vn is the Nyquist velocity, which can be read from the Doppler blue and red-yellow velocity display scale.

Maximal accelerating flow rate. Both maximal accelerating flow rate from two-dimensional Doppler color mapping (Fig. 1) and that from Doppler color M-mode recording (Fig. 2) were obtained. In the Doppler color two-dimensional recording, the maximal radius (r) of the hemisphere was measured from the maximal distance between the first aliasing boundary and the entrance of the regurgitant orifice at the frame showing maximal proximal accelerating region through frame by frame searching (Fig. 1). In the Doppler color M-mode echocardiogram, the maximal distance between the first aliasing boundary and the mitral leaflet leading edge (Fig. 2) was defined as the maximal radius (r) of the isovelocity hemisphere. The maximal accelerating flow rate was then calculated with equation 1.

Mean accelerating flow rate and stroke accelerating flow volume. These were calculated using Doppler color M-mode recording. The area of the proximal accelerating region was defined by the area between the first aliasing boundary and the mitral leaflet leading edge during systole in Doppler color M-mode echocardiogram. Mean radius (height) was calculated by dividing the proximal accelerating area by duration (d, width) of the region (Fig. 2). Mean accelerating flow rate was then calculated with equation 1. Stroke accelerating flow volume was calculated by multiplying the mean accelerating flow rate by systolic time.

Catheterization and angiography. Left ventriculography was performed in all patients in the 30° right anterior oblique projection with the injection of 40 to 50 ml meglomine diatrizoate (Renografin) at 13 to 16 ml/s. The severity of mitral regurgitation was graded from I to IV (mild to severe) according to the classification of Sellers et al. (29). The angiograms were interpreted by consensus of two observers who did not know the results of the Doppler color study evaluation. The interval between angiography and echocardiographic examination was 1 day to 2 months.

Reproducibility study. Pulsed wave Doppler and two-dimensional echocardiographic calculations of mitral inflow and aortic forward flow were performed in 20 patients without mitral regurgitation or other valve diseases. The interobserver variability of regurgitant flow rate in patients with mitral regurgitation was also examined by two independent observers. To test the reproducibility of calculation of proximal accelerating flow, measurements of the proximal accelerating flow variables were examined by the same observer in 10 patients after an interval of 2 weeks.

Statistical analysis. All values were expressed as mean value ± SD. Linear regression was used to compare pulsed wave Doppler and Doppler color study assessments of mitral regurgitation. For these analyses, the mean or the maximal Doppler color proximal accelerating flow rate and the accelerating stroke volume were the dependent variables; the independent variables tested included the regurgitant flow rate and the stroke regurgitant volume. The relation between angiographic severity of mitral regurgitation and the mean regurgitant flow rate or the accelerating flow rate was also examined using the Spearman rank-order correlation. Differences between the Doppler color accelerating flow and the pulsed wave regurgitant flow variables were examined with the Student *t* test. One way analysis of variance (ANOVA) was used to examine the influence of different causes of regurgitation on the difference between the mean regurgitant flow rate and the mean accelerating flow rate

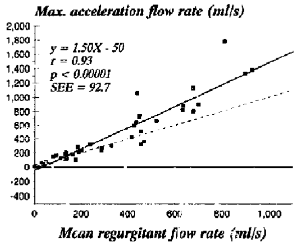


Figure 3. Correlation between the regurgitant flow rate and the maximal (Max.) accelerating flow rate from the Doppler color M-mode recording. The mean regurgitant flow is overestimated by the maximal accelerating flow (away from the dashed line, which is the line of identity).

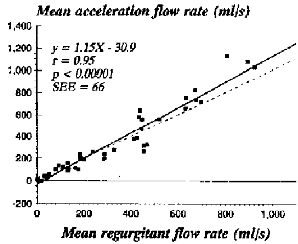


Figure 4. Correlation between the regurgitant flow rate and the mean accelerating flow rate from Doppler color M-mode recording. The regression line is close to the line of identity (dashed line).

(Table 1). A p value of < 0.05 was considered statistically significant.

Results

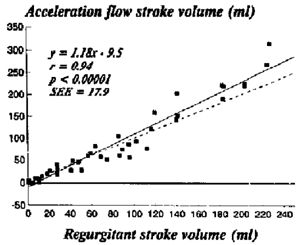
The mean heart rate was 80 ± 16 beats/min and the mean left ventricular ejection fraction was 51 ± 15% (range 20% to 70%). By angiography, mitral regurgitation was grade I in 11 patients, grade II in 10, grade III in 10 and grade IV in 15. The stroke regurgitant volume was 76.06 ± 59.76 ml and the mean regurgitant flow rate was 306 ± 253 ml/s.

The proximal accelerating flow region was observed in 42 of 46 patients. When considering severity of mitral regurgitation, all patients with mitral regurgitation of grade II or higher had a proximal accelerating flow observed at an aliasing velocity of 49 to 58 cm/s. Only 7 (64%) of 11 patients with grade I regurgitation showed a visible proximal accelerating flow region at the aliasing velocity of 49 to 58 cm/s. Four patients without a visible proximal accelerating flow region had a regurgitant flow rate of ≤18 ml/s and a stroke regurgitant volume of ≤4.5 ml.

Doppler color proximal accelerating flow and mitral regurgitant flow. Although there was a good correlation between the mean regurgitant flow rate and the maximal Doppler color M-mode accelerating flow rate (Fig. 3), the maximal accelerating flow rate (406 ± 421 ml/s) was slightly but significantly higher than the mean regurgitant flow rate (306 ± 253 ml/s, $p < 0.03$). Likewise, the maximal Doppler color two-dimensional proximal accelerating flow rate (372 ± 389 ml/s) was significantly higher than the mean regurgitant flow rate (306 ± 253 ml, $p < 0.05$) although the correlation between the two variables was good ($r = 0.93$, $p < 0.00001$). As shown in Figure 3, the overestimation of mean regurgitant flow by the maximal accelerating flow rate was most obvious when the regurgitant flow rate was >300 ml/s. The mean Doppler color M-mode proximal accelerating flow rate was 318 ± 304 ml/s and did not differ from the regurgitant flow rate (306 ± 253, p = NS). The mean Doppler color flow rate correlated well with the mean regurgitant flow rate ($r = 0.95$, $p < 0.00001$; Fig. 4). However, there were significant data scatter and a tendency toward overestimation of the regurgitant flow rate by the mean accelerating flow rate when mitral regurgitation was more severe, with the regurgitant flow rate >300 ml/s (Fig. 4).

The stroke accelerating flow volume correlated well with regurgitant flow stroke volume ($r = 0.94$, $p < 0.00001$; Fig. 5). There were an obvious data scatter and a tendency toward overestimation of the regurgitant stroke volume by the accelerating stroke volume when regurgitant stroke volume was >60 ml (Fig. 5). In the entire study group, the mean accelerating flow volume (78.27 ± 62.72 ml) was slightly greater than the regurgitant stroke volume (76.06 ± 59.76 ml), but the difference was not significant (p = NS).

Figure 5. Correlation between the regurgitant flow stroke volume and the accelerating flow stroke volume calculated from Doppler color M-mode recording. The regression line was not different from the line of identity (dashed line).



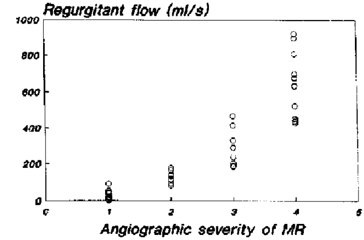


Figure 6. Relation between the regurgitant flow rate and the angiographic grade of mitral regurgitation (MR). There was significant overlap of data among the subgroups.

Regurgitant flow rate and angiographic severity of mitral regurgitation. The correlation between angiographic semiquantitative grading of mitral regurgitation and regurgitant flow rate is presented in Figure 6. Although there was a relatively good correlation ($r = 0.89$, $p < 0.001$), regurgitant flow rate varied from 427 to 925 ml/s (mean 609 ± 165) for grade IV mitral regurgitation, from 156 to 468 ml/s (mean 278 ± 95) for grade III, from 80 to 175 ml/s (mean 129 ± 28) for grade II and from 0 to 90 ml/s (mean 31 ± 26) for grade I mitral regurgitation.

Likewise, there was a strong correlation ($r = 0.88$, $p < 0.001$) between the maximal accelerating flow derived from the color M-mode recording and severe grades of mitral regurgitation (Fig. 7). A significant overlap of regurgitant flow rate among groups exists (Fig. 7). Slightly less overlap of the regurgitant flow rate was observed between patients with grade IV mitral regurgitation and those with less severe regurgitation. An averaged regurgitant flow rate of grade IV mitral regurgitation (899.8 ± 364.7 ml/s) was almost three times higher than that (297.7 ± 57.8 ml/s) of grade III regurgitation. Although the maximal accelerating flow rate in grade IV mitral regurgitation varied greatly from 324 to 1,768 ml/s, all except one patient with this degree of regurgitation had a regurgitant flow rate >400 ml/s.

Figure 7. Relation between the maximal (Max.) accelerating flow rate from Doppler color M-mode recording and the angiographic grade of mitral regurgitation (MR). Note the significant overlap among the subgroups.

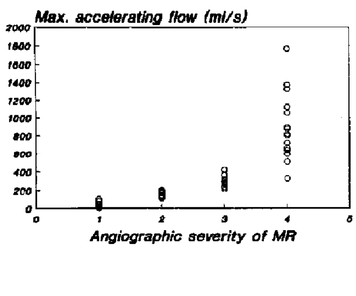


Table 1. Comparison of Mean Proximal Accelerating Flow and Mean Regurgitant Flow Rate in Mitral Regurgitation of Various Causes

	Mean Flow Rate (ml/s)	
Cause of Regurgitation	Regurgitant	Accelerating
Coronary artery disease	251 ± 218	244 ± 225
Dilated cardiomyopathy	125 ± 82	123 ± 75
Mitral valve prolapse	221 ± 185	262 ± 271
Rupture chordae	588 ± 213	563 ± 239
Others	445 ± 318	493 ± 346

Values are expressed as mean value ± SD.

Factors affecting the correlation of the proximal accelerating flow with the regurgitant flow. Analysis of variance reveals that the difference of the mean accelerating flow rate from the mean regurgitant flow rate did not relate significantly to the causes of mitral regurgitation ($p = 0.1$) (Table 1). Although mitral valve prolapse tended to overestimate the mean regurgitant flow rate using the mean proximal accelerating flow rate, the difference was not statistically significant (p = NS).

Reproducibility. Correlations between measurements performed by the same observer 2 weeks apart were excellent for all proximal accelerating flow measurements: $r = 0.98$ and $p < 0.001$ for the maximal proximal accelerating flow rate, mean accelerating flow rate and accelerating flow volume by Doppler color M-mode recording and $r = 0.95$, $p < 0.001$ for the maximal proximal accelerating flow rate by Doppler color two-dimensional mapping. The mean percent differences between intraobserver measurements were 9.6 ± 2.3% for the maximal Doppler color two-dimensional proximal accelerating flow rate (252 ± 150 vs. 279 ± 160 ml/s), 7.8 ± 2.1% for maximal Doppler color M-mode proximal accelerating flow rate (258 ± 144 vs. 280 ± 150 ml/s) and 6.9 ± 2.0% for mean M-mode proximal accelerating flow rate (215 ± 123 vs. 231 ± 143 ml/s). Mitral inflow correlated well with aortic forward flow measured in normal subjects ($r = 0.96$, $p < 0.001$). There was no significant difference between mitral (5,284 ± 404 ml/min) and aortic (5,345 ± 365 ml/min) flow in normal subjects (p = NS). The reproducibility of measurements of mitral regurgitant flow rate was also excellent with a close correlation ($r = 0.97$, $p < 0.001$) between two measurements (228 ± 124 ml/s vs. 237 ± 130 ml/s, p = NS) by two observers.

Discussion

Measurements of mitral regurgitant flow rate and volume have been limited in clinical routine because of the complexity of the methodologies. The results of the present study demonstrate that mitral regurgitant flow rate and volume can be reliably estimated by using proximal accelerating flow field in most patients with regurgitation of various causes although regurgitant flow is slightly overestimated by the accelerating flow calculation. The proximal accelerating method of measurement of mitral regurgitant volume and flow rate provides a simple method for noninvasive quantitative assessment of severity of mitral regurgitation and thus may have important clinical and research applications, especially in assessing effects of medical and surgical interventions on severity and natural history of mitral regurgitation.

Semiquantification of mitral regurgitation. Angiographic semiquantitative grading of severity of mitral regurgitation is used widely in routine clinical settings and considered the reference standard in the absence of a more reliable method that can be used for daily patient care (29,30). This semiquantitative grading approach provides valuable information for identifying severe mitral regurgitation and has been used for clinical decision making. However, this method is subjective and affected by many variables, including catheter position, amount and velocity of contrast agent injected, chamber size, forward flow through the aortic valve, radiogram penetration and rhythm disturbances (30,31).

Noninvasive mapping of regurgitant jet extension in the left atrium, studied either with pulsed wave Doppler study or Doppler color flow mapping, is used to estimate severity of mitral regurgitation. Not only regurgitant flow rate and volume determine jet extension; other factors, such as echocardiographic machinery settings, wall impingement of the regurgitant jet, difference between left atrial and ventricular pressures, regurgitant orifice size and left atrial dimension, affect jet dimension and geometry of spatial distribution (2–11). Therefore, mapping of jet extension offers only semiquantitative information about the severity of mitral regurgitation under certain controlled circumstances.

All systems used for semiquantitative assessment of mitral regurgitation have only limited ability to distinguish mild to moderate change in severity of mitral regurgitation. In patients with grade IV mitral regurgitation, regurgitant flow rate can vary as much as 498 ml/s (from 427 to 925 ml/s), which is 82% of the average flow rate (609 ml/s) of the patients who had grade IV mitral regurgitation as defined by angiography in this study. Similar results were reported in previous studies (31). There was also significant overlap among subgroups. Therefore, for precise assessment of interventional effect on severity of mitral regurgitation, a more precise and quantitative method of mitral regurgitation is required.

Conventional quantification of mitral regurgitation. Angiographic quantitative technique uses left ventricular stroke volume calculated from the left ventriculogram for total mitral inflow (effective forward flow and regurgitant flow) and Fick or thermodilution stroke volume for effective forward flow (30–32). The measurement error for cardiac output is between 5% and 10% for thermodilution and between 10% and 15% for angiography (32), resulting in an even greater error when they are combined into the mitral regurgitant fraction or volume. Furthermore, this method cannot be used in patients with atrial fibrillation and extrasystoles during angiography and it is not suitable for patients with aortic regurgitation.

Pulsed wave Doppler echocardiography has been used to calculate mitral regurgitant volume, regurgitant flow rate and regurgitant fraction (6,26,33,34). The total mitral inflow can be calculated by multiplying the velocity-time integral of the diastolic mitral velocity spectrum at the mitral leaflet tip and mitral valve area as described under Methods (6,26,33). The alternative method for calculating mitral inflow is by taking the velocity integral at the mitral anulus and mitral anulus area (34). The effective forward flow is measured from the aortic anulus level. The difference between aortic forward flow and mitral inflow obtained with the Fisher method for patients without mitral regurgitation was −6% to +9% of mitral flow in our previous study (6) and was as high as 14% in other studies (33–35). The accuracy of the regurgitant flow rate and fraction calculated with this method has been validated in a canine model (6,26) against the true regurgitant flow. However, this method is rather time-consuming (45 min for each study and analysis) with the current commercially available echocardiographic equipment, requires expertise in acquiring and analyzing data and is not suitable for patients with multivalvular disease. Therefore, the combining method of pulsed wave Doppler and two-dimensional and M-mode data has not been used in most laboratories routinely.

Proximal accelerating flow field. The proximal acceleration region observed in Doppler color flow mapping can be used not only to identify more than mild mitral regurgitation but also to provide quantitative measurements of severity of mitral regurgitation. Bargiggia et al. (19) observed proximal acceleration in 86% of patients with mitral regurgitation. Visibility of flow acceleration proximal to a regurgitant orifice by Doppler color flow mapping depends on the severity of mitral regurgitation (regurgitant flow rate). Patients with very mild mitral regurgitation and a regurgitant flow rate of <20 ml/s or a stroke regurgitant volume of ≤ 4.5 ml did not have a visible proximal acceleration zone at a Nyquist velocity of 49 to 58 cm/s in this study. Certainly, a lower Nyquist velocity setting will increase the sensitivity for detecting trivial proximal flow accelerating field.

Accelerating flow rate versus regurgitant flow rate. A close correlation between angiographic grading of mitral regurgitation and maximal accelerating flow rate calculated from proximal accelerating flow was demonstrated by Bargiggia et al. (19) ($r = 0.91$, $p < 0.001$) and in our previous study (25) ($r = 0.89$, $p < 0.001$). The present study demonstrated that although the maximal flow rate calculated from the proximal accelerating field correlated well with regurgitant flow rate averaged through systole, there was a significant overestimation of regurgitant flow by the maximal accelerating flow rate. This may be due to variation in mitral regurgitant orifice size and pressure gradient between the left atrium and the regurgitant flow rate during systole as suggested in Figure 2.

The Doppler color M-mode recording of the proximal accelerating region provides integration of regurgitant flow throughout systole. Using Doppler color two-dimensional guided M-mode recording of proximal acceleration region, we demonstrated a strong correlation between the mean accelerating flow rate and mean regurgitant flow rate (r = 0.95). The mean accelerating flow rate tended to be slightly higher than the regurgitant flow rate, especially at a higher regurgitant flow rate. Likewise, stroke accelerating flow volume calculated from Doppler M-mode recording accurately predicts the regurgitant stroke volume, but the data scattered when the regurgitant flow stroke volume was >60 ml. There is a theoretic possibility of underestimating regurgitant volume or flow rate by off angle of Doppler color flow mapping or flat shape of the isovelocity layer near the regurgitant orifice. Why the mean accelerating flow rate on Doppler color study, especially at the higher regurgitant flow rate, tends to slightly overestimate regurgitant flow rate is not clear. It is possible that the isovelocity layers do not have a hemispheric shape when at a great distance from the regurgitant orifice (36); this hypothesis requires further investigation (37). Theoretically, the existing intraventricular flow, which is destined to pass the left ventricular outflow tract, could supperimpose the proximal accelerating flow through the mitral regurgitant orifice, especially when the regurgitant orifice is near the left ventricular outflow tract. If one uses the hemispheric model to calculate the proximal accelerating flow, it is possible that higher interventricular flow could lead to overestimation of the regurgitant flow by the proximal accelerating flow. The regurgitant orifice, which is close to the left ventricular wall, could also influence the accuracy of the proximal accelerating flow calculation by which the ventricular wall may distort hemispheric shape of the proximal flow convergent isovelocity layers. This may be especially true for a small left ventricular cavity during systole. All of these possibilities require further investigations.

Technical factors in flow rate measurements. It is important to discuss some technical points concerning accuracy of measurements of regurgitant flow rate or volume using Doppler color flow mapping of the proximal accelerating flow region. 1) Temporal and spatial (axial and lateral) resolutions of two-dimensional Doppler color flow mapping are dependent on the size and depth of the imaging area and the frequency of the transducer chosen. Whenever possible, the narrowest imaging angle, shallowest depth, highest imaging frequency and lowest pulse repetition frequency should be chosen to increase the resolutions of Doppler color mapping (16). 2) The proximal accelerating field should be magnified as large as possible to minimize measurement error. 3) The prerequisite for accurate measurement of the proximal accelerating flow is to be able to record the largest proximal accelerating area using two-dimensional scanning through both standard and nonstandard imaging planes with a rotating, shifting and angulating imaging transducer. 4) To distinguish low interventricular flow from true proximal accelerating flow, Nyquist limit velocity should not be reduced too low because it may be confused with the interventricular low velocity flow, although a higher Nyquist limit will lead to underestimation of regurgitant flow because isovelocity layers near the regurgitant orifice no longer appear hemispheric. In the present study, the Nyquist velocity selected was 19 to 39 cm/s (mostly 27 to 39 cm/s) and appeared appropriate. 5) The M-mode beam should be aligned center to the accelerating region and perpendicular to the regurgitant orifice plane. This requires a learning period and experience. We did not use data from our learning period in this study. However, even with an experienced echocardiographer, it is not always possible to align the M-mode beam appropriately.

Limitations of the study. There is no satisfactory method for quantifying mitral regurgitant volume and flow rate. Both methods currently available for quantifying mitral regurgitation—angiography and a combination of pulsed wave Doppler and two-dimensional echocardiography—have methodologic limitations and systematic error (6,26–28,30,31). However, systematic error should not bias the correlations of this study. Because there was no simultaneous measurement of angiographic regurgitant flow, we chose the Fisher method for measuring mitral inflow and aortic anulus flow for measurement of aortic forward flow. These methods are validated independently against true regurgitant flow in a canine model (26), and clinical studies (33,35) showed that these methods have the least measurement variation. Because distance required for an accelerating isovelocity flow layer away from regurgitant orifice to be hemispheric is dependent on both orifice diameter and Nyquist velocity (20), an extremely large regurgitant orifice as that produced by rupture of mitral chordal apparatus may cause underestimation of accelerating flow with the hemispheric model. By using Nyquist velocity (19 to 39 cm/s) in this study, the mean accelerating flow rate was not different from the regurgitant flow rate. However, a larger number of patients is required to reach a definite conclusion. In one patient, the regurgitant flow rate of 456 ml/s was significantly underestimated by the mean accelerating flow rate (264 ml/s). Surface morphology of mitral leaflets could theoretically also significantly alter the accuracy of accelerating flow calculation (37).

Patients with mitral valve prolapse. In this study, patients with mitral valve prolapse tended to have a higher mean rate of accelerating than of regurgitant flow, but there was no significant difference, probably because of the small number of patients. In the presence of mitral valve prolapse, we were especially careful to image proximal accelerating flow with its entrance to the regurgitant orifice and both sides of mitral leaflets. As a result, significant overestimation was observed in only one of five patients who had an actual regurgitant flow rate of 809 ml/s, which was 39% lower than the mean accelerating flow rate (1,123 ml/s) and 54% lower than the maximal accelerating flow rate (1,768 ml/s). This may be because the entrance of the regurgitant orifice has a tunnel shape and the regurgitant flow developed only at late systole in this case. Therefore, further studies with a larger number of patients are required to examine the applicability of the proximal accelerating flow method for estimating regurgitant flow in patients with severe mitral valve prolapse. Location of the mitral regurgitant orifice near the left ventricular outflow tract could theoretically lead to overestimation of the regurgitant flow by the accelerating flow (18), although this was not encountered in this study.

Clinical implications. Proximal accelerating flow field provides a novel approach for quantifying mitral regurgitation. This method could be most useful in patients with eccentrically directed wall-impinging regurgitant jets, in which jet size in the left atrium on Doppler color flow mapping is not reliable for estimating severity of mitral regurgitation (6). This method could also be useful for assessing and following up effects of medical interventions, such as vasodilating agents to reduce systemic vascular resistance, on regurgitant flow rate and volume and these effects on the natural history of mitral regurgitation.

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References

1. Weyman AE. Cross-sectional echocardiography. Philadelphia: Lea & Febiger, 1982:139.
2. Omoto R, Yokote Y, Takamoto S, et al. The development of real time two-dimensional Doppler echocardiography and its clinical significance in acquired valvular diseases: with special references to the evaluation of valvular regurgitation. Jpn Heart J 1984;25:325–40.
3. Miyatake K, Izumi S, Okamoto M, et al. Semiquantitative grading of severity of mitral regurgitation by real-time two-dimensional Doppler flow imaging technique. J Am Coll Cardiol 1986;7:82–8.
4. Helmcke F, Nanda NC, Hsuin MC, et al. Color Doppler assessment of mitral regurgitation with orthogonal planes. Circulation 1987;75:175–83.
5. Spain MG, Smith MD, Grayburn PA, Harlamert EA, DeMaria AN. Quantitative assessment of mitral regurgitation by Doppler color flow imaging: angiographic and hemodynamic correlations. J Am Coll Cardiol 1989;13:585–90.
6. Chen C, Thomas JD, Anconina J, et al. Impact of impinging wall jet on color Doppler quantification of mitral regurgitation. Circulation 1991;84:712–20.
7. Mohr-Kahaly S, Lotter R, Bremecke R. Influence of color Doppler instrument set-up on the minimal encoded velocity. An in vitro study (abstr). Circulation 1988;78(suppl II):II-12.
8. Maurer G, Czer LSC, Chaux Aurelio, et al. Intraoperative Doppler color flow mapping for assessment of valve repair for mitral regurgitation. Am J Cardiol 1987;60:333–7.
9. Shah PM. Quantitative assessment of mitral regurgitation. J Am Coll Cardiol 1989;13:591–3.
10. Simpson IA, Sahn DJ. Hydrodynamic investigation of a hemodynamic problem: a review of the in vitro evaluation of mitral insufficiency by color Doppler flow mapping. J Am Soc Echocardiogr 1989;2:67–72.
11. Sahn DJ. Instrumentation and physical factors related to visualization of stenotic and regurgitant jets by Doppler color flow mapping. J Am Coll Cardiol 1988;12:1354–65.
12. Sahn DJ, Simpson IA, Murillo A, Valdes-Cruz LM. Observations of acceleration proximal to restrictive orifices in congenital heart diseases: important clues for the interpretation of Doppler color flow maps (abstr). Circulation 1988;78(suppl II):II-649.
13. Bargiggia GS, Recusani F, Yoganathan AP, et al. Color flow Doppler quantitation of regurgitant flow rate using the flow convergence region proximal to the orifice of a regurgitant jet (abstr). Circulation 1988;78(suppl II):II-609.
14. Utsunomiya T, Ogawa T, Tang HA, Henry WL, Gardin JM. Doppler color flow mapping of the "proximal" isovelocity surface area": a new method for measuring volume blood flow across an orifice (abstr). J Am Coll Cardiol 1989;13(suppl A):225A.
15. Rodriguez L, Vlahakes GJ, Yoganathan AP, Guerrero JL, Levine RA. Quantification of regurgitant flow rate using the proximal flow convergence method: in vivo validation (abstr). Circulation 1989;80(suppl II):II-570.
16. Recusani F, Bargiggia GS, Yoganathan AP, et al. A new method for quantification of regurgitant flow rate using color flow Doppler imaging of the flow convergence region proximal to a discrete orifice: in vitro study and initial clinical experience in patients with mitral insufficiency. Circulation 1991;83:594–604.
17. Moises VA, Maciel B, Hornberger LK, et al. A new method for noninvasive estimation of ventricular septal defect shunt flow by Doppler color flow mapping: imaging of the laminar flow convergence region on the left septal surface. J Am Coll Cardiol 1991;18:824–32.
18. Levine RA. Doppler color mapping of the proximal flow convergence region: a new quantitative physiological tool. J Am Coll Cardiol 1991;18:833–6.
19. Bargiggia GS, Tronconi L, Sahn DJ, et al. A new method for quantitation of mitral regurgitation based on color flow Doppler imaging of flow convergence proximal to regurgitant orifice. Circulation 1991;84:1481–9.
20. Rodriguez L, Anconina J, Harrigan P, et al. Nyquist limit and orifice area independently affect the accuracy of proximal isovelocity surface area estimation of flow rate: an in vitro study (abstr). J Am Coll Cardiol 1990;15(suppl A):109A.
21. Cape EG, Yoganathan AP, Rodriguez L, Weyman AE, Levine RA. The proximal flow convergence method can be extended to calculate regurgitant stroke volume: in vitro application of the color Doppler M-mode (abstr). J Am Coll Cardiol 1990;15(suppl A):109A.
22. Walker PG, Cape EG, Pohost GM, Cranney GB, Yoganathan AP. Regurgitant orifice isovelocity contour mapping using NMR velocity encoding. Circulation 1990;82(suppl III):III-63.
23. Rouse H. Fluid Mechanics for Hydraulic Engineers. New York: Dover, 1961:83–95.
24. Blevins RD. Applied Fluid Dynamics Handbook. New York: Van Nostrand Reinhold, 1984:229–41.
25. Chen C, Koschyk D, Mehl C, Klarhoefer M, Kupper W, Bleifeld W. Comparison of quantifying mitral regurgitation using color Doppler proximal isovelocity surface area and angiography. Circulation 1991;84(suppl II):II-637.
26. Ascah KJ, Stewart WJ, Jiang L, et al. A Doppler-two-dimensional echocardiographic method for quantitation of mitral regurgitation. Circulation 1985;72:377–83.
27. Stewart WJ, Palacios I, Jiang L, Dinsmore RE, Weyman AE. Doppler measurement of regurgitant fraction in patients with mitral regurgitation: a new quantitative technique (abstr). Circulation 1983;68(suppl III):III-111.
28. Fisher DC, Sahn DJ, Friedman JM, et al. The mitral valve orifice method for noninvasive two-dimensional echo Doppler determination of cardiac output. Circulation 1983;67:872–7.
29. Sellers RD, Levy MJ, Amplatz K, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease: technic, indications and interpretations in 700 cases. Am J Cardiol 1964;14:437–47.
30. Dodge HT, Hay RE, Sandler H. An angiographic method for directly determining left ventricular stroke volume in man. Circ Res 1962;11:739–45.
31. Croft CH, Lipscomb K, Mathis K, et al. Limitation of qualitative angiographic grading in aortic or mitral regurgitation. Am J Cardiol 1984;53:1593–8.
32. Fifer MA, Grossman W. Measurement of left ventricular volumes, ejection fraction, mass, and wall stress. In: Grossman W, ed. Cardiac Catheterization and angiography. Philadelphia: Lea & Febiger, 1986;282–300.
33. Zhang Y, Ihlen H, Myhre E, Levorstad K, Nitter-Hauge S. Measurement of mitral regurgitation by Doppler echocardiography. Br heart J 1985;54:384–91.

34. Rokey R, Sterling LL, Zoghbi WA, et al. Determination of regurgitant fraction in isolated mitral or aortic regurgitation by pulsed Doppler two-dimensional echocardiography. J Am Coll Cardiol 1986;7:1273–8.
35. Dittmann H, Voelker W, Karsch KR, Seipel L. Influence of sampling site and flow area on cardiac output measurements by Doppler echocardiography. J Am Coll Cardiol 1987;10:818–23.
36. Barclay SA, Changsheng X, Loyd D, Andersson G, Ask P, Wranne B. The flow convergence region proximal to a regurgitant orifice has a non-hemispherical velocity field. Circulation 1991;84(suppl II):II-105.
37. Levine RA, Rodriguez L, Cape EG, et al. The proximal flow convergence method for calculating orifice flow rate requires correction for surrounding leaflet geometry. J Am Coll Cardiol 1991;17(suppl A):359A.